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Study of behavioral modifications resulting from Exposure to high LET indication

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FINAL REPORT

STUDY OF BEHAVIORAL MODIFICATIONS RESULTING FROM EXPOSURE TO HIGH LET RADIATION

Contract No. NAS9-16375

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FINAL REPORT

Study of Behavioral Modifications Resulting from Exposure to High LET Radiation

Contract Number NAS9-16375

31 January 1983

I. INTRODUCTION

This document constitutes the final report of studies performed under Contract No. NAS9-16375. Due to circumstances beyond the control of NASA and Texas A&M University, modifications of the contract were required concerning the scope of work. The RFP and original response to it required the irradiation of animals with HZE particles from the BEVALAC accelerator at the University of California. When this was not possible, dogs were irradiated with the gamma rays from a Cobalt-60 therapy source in the College of Veterinary Medicine. It is this study that will be reported herein.

For ease of presentation, this report has been subdivided into the following parts:

- I. Introduction
- II. Animal Irradiations
- III. Behavioral Studies
 - IV. Neurologic Studies
 - V. Nuclear Medicine Studies
- VI. Conclusions
- VII. Recommendations

While the report is written in sections, it is to be noted that the performance of the studies was an integrated effort. In addition, as a contract requirement, a bibliography concerning radiation effects and

behavioral change has been prepared as a separate document.

II. ANIMAL IRRADIATION

Six beagle docs were irradiated on September 3, 1982. The radiation source was the Cobalt-60 teletherapy unit used for radiation therapy in the Veterinary Teaching Hospital. The dogs were divided into two groups. One group of six dogs were to be the control group. The other six dogs were further divided into two groups of three dogs each. One group received 1000 rads to the midline of the brain and the other 1750 rads.

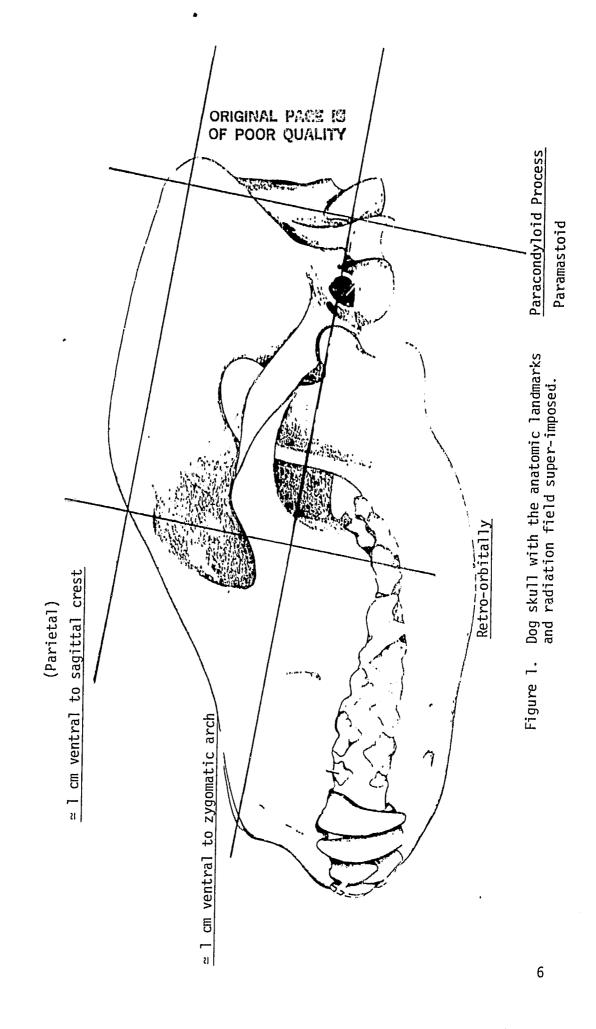
Dogs to be irradiated were lightly anesthetized with sodium pentobarbital. They were placed in a sling holder for irradiation. Controls were similarly anesthetized and sham irradiated.

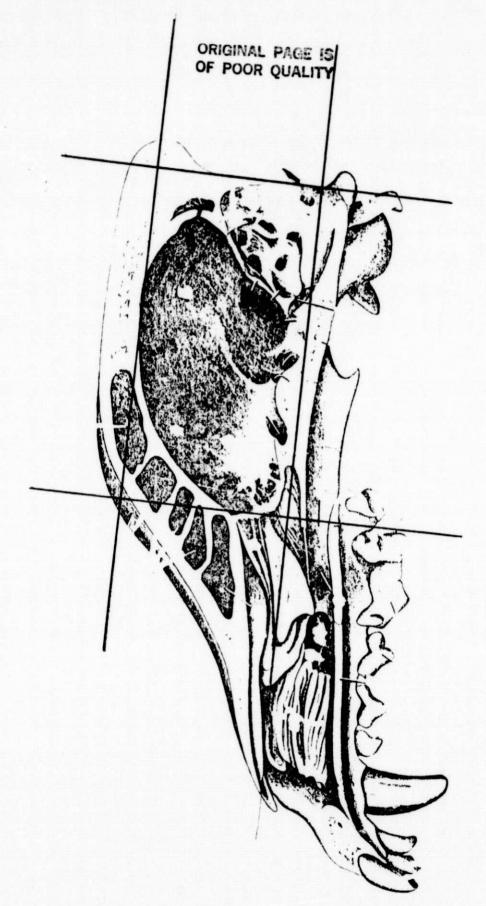
Irradiation was performed with lateral opposing fields to the head. Each field was approximately 7.5 cm high by 10 cm long at a source to skin distance of 80 cm. Figures 1 and 2 illustrate the external "landmarks" used to position the animal and the inner structure of the head that we irradiated.

Very little variation in head thickness was determined between different animals. Thus, an average skin-to-midline depth of 4.38 cm was used for all calculations. Correction for bone attenuation was made assuming a 0.6 cm thick cranium. Tissue equivalent bolus was used when necessary to compensate for irregular head shape. A Victoreen Model 05-595 portable therapy dosimeter with a silicon diode detector (Model 30-490) was used to verify dose received at midfield on the surface.

The equation and parameter values required for calculation of the dose rate were taken from "The Physics of Radiology", Johns, H.E. and Cunningham, J.R., Charles C. Thomas Publisher, 1974. These are defined as follows:

$$\dot{D} = (\dot{X}) (A_{eq}) (f_{tissue}) (BSF) (%DD) (C_{bone})$$
where





Sagittal section of the skull with the radiation field super-imposed. Figure 2.

- \dot{D} = dose rate at 4.38 cm depth, 7.5 x 10 cm field, 80 cm SSD from 60 Co gamma rays $(\frac{\text{rads}}{\text{min}})$
- \dot{X} = exposure rate in air at 80.5 cm from source decay corrected to 9/3/82 (R/min)

 A_{eq} = Equilibrium air attenuation factor (0.985 for 60 Co) f_{tissue} = rads/Roentgen conversion factor in tissue for 60 Co) (0.957 rads/R)

BSF = Back scatter factor for 60 Co field, 7.5 x 10 cm (1.031) %DD = Percent depth dose at 4.38 cm for 60 Co field, 7.5 x 10 cm

(0.80859)

 C_{bone} = Correction factor for 0.6 cm bone attenuation (0.979) These calculations were used to determine a dose rate of 55.931 rads/min. Total dosages delivered to each dog are shown in Table 1.

III. BEHAVIORAL STUDY

A. Twenty-Four Hour Activity Patterns.

Each of the twelve dogs was videotaped for twenty-four consecutive hours prior to radiation, approximately four weeks post-radiation, and approximately twelve weeks post-radiation. The videotapes of the three dogs receiving the heavy doses of radiation were evaluated to determine the amount of time each dog spent moving, standing, sitting, and lying while in a 4 x 10 foot kennel area. Times in these activities were recorded to the nearest 10 seconds. In addition, the number of times each dog made major changes between these four activities was counted, as was the number of times each jumped up against the wire walls. Total times calculated for each dog, as found in Table 2, do not equal twenty-four hours because time spent in other activities such as grooming, eating, and eliminating were not included. The pre-radiation data from each dog was used to compare with activity data gathered after radiation.

Table 1

Dog Number and Radiation Dose Delivered

| Dog No. | Target Dose (rads) | Actual Dose (rads) | Error |
|---------|--------------------|--------------------|-------|
| 3 | 1750 | 1740 | -0.6 |
| 6 | 1750 | 1723 | -1.5 |
| 7 | 1750 | 1737 | -0.7 |
| 5 | 1000 | 994 | -0.6 |
| 8 | 1000 | 1009 | +0.9 |
| 10 | 1000 | 999 | -0.1 |

Table 2
Twenty-Four Hour Activity Patterns*

| | | Jumping (count) | Moving (min) | Standing (min) | Sitting (min) | Lying (min) | Changes in Behavior (count) |
|------------|----------------|--------------------|-----------------|----------------|------------------|----------------|-----------------------------------|
| Pre-Radiat | ion Observatio | กย | | | | | |
| Llog # | 3 | 23 | 223.0 | 16.8 | 48.0 | 1094.5 | 389 |
| # | 16 | 12 | 166.2 | 99.7 | 33.7 | 1096.2 | 663 |
| # | 1 7 | 88 | 270.0 | 149.7 | 122.7 | 558.8 | 666 |
| 4 Weeks Po | st-Radiation O | bservati | ons | | | | |
| Dog # | :3 | 48 | 142.0 | 82.0 | 93.3 | 926.7 | 377 |
| # | 6 | 10 | 154.8 | 123.7 | 53.5 | 953.5 | 472 |
| # | 7 | 10 | 90.7 | 60.5 | 85.3 | 1082.5 | 313 |
| 12 Weeks P | ost-Radiation | Observat | ions | | | | |
| Dog # | 3 | 11 | 151.7 | 25.7 | 435.0 | 624.2 | 385 |
| # | 6 | 53 | 166.3 | 244.2 | 234.5 | 756.3 | 620 |
| # | 7 | 87 | 237.5 | 107.5 | 262.5 | 731.3 | 437 |

^{*}Times do not add up to 24 hours because of behaviors performed which are not included in those listed.

In that way each dog served as its own control.

Since there was some discrepancy in total times observed between dogs, each of the four behaviors was calculated as a certain percentage of the observed time. For example, in the initial phase of the study, dog 3 moved 223 minutes, stood 16.8 minutes, sat 48 minutes, and laid 1094.5 minutes, for a total observed time of 1381.3 minutes (23.0 hours). Of this recorded time, 16.13% was spent moving, 1.22% was standing, 3.47% was sitting, and 79.18% was lying. Table 3 shows the comparative percentage data between the three dogs and the three observations of each.

If there was no change in a dog's activity between each test, the numbers of Table 3 should be approximately the same, and in fact in some instances, this is the case. Table 4 makes a comparison between the post-radiation data and that gathered in the control study. To obtain the figures of Table 3, the percent of time spent on an activity in tests 2 and 3 was divided by the parcent of time spent on the same activity during the control observation. A correlation of 1.0 would mean that the two pieces of data were identical. A number less than 1.0 indicates that the dog spent less time doing the activity after radiation, and a number greater than 1.0 would signify the opposite.

For dog 3 obvious time differences include the following:

Test 2 - increases in standing (66 minutes) and sitting (45 minutes)

- decreases in walking (81 minutes)

Test 3 - increases in standing (9 minutes) and sitting (387 minutes)

- decreases in walking (71 minutes) and lying (470 minutes)

For dog 6 the differences are as follows:

Test 2 - increases in standing (24 minutes) and sitting (20 minutes)

Table 3

Percentage of Recorded Time Spent in Specific Activities

| | | Moving (%) | Standing (%) | Sitting (%) | Lying (%) |
|------------------------------------|-------------|------------------|--------------|-------------|-----------|
| Pre-Radia | ation Obser | vations | | | |
| Dog | #3 | 16.13 | 1.22 | 3.47 | 79.18 |
| | #6 | 11.91 | 7.14 | 2.41 | 78.54 |
| | #7 | 24.52 | 13.59 | 11.14 | 50.75 |
| 4 Weeks Post-Radiation Observation | | | | | |
| Dog | #3 | 11.41 | 6.59 | 7.50 | 74.49 |
| | #6 | 12.04 | 9.62 | 4.16 | 74.17 |
| | #7 | 6.87 | 4.59 | 6.47 | 82.07 |
| 12 Weeks | Post-Radia | tion Observation | 5 | | |
| Dog | #3 | 12.27 | 2.08 | 35.18 | 50.48 |
| | #6 | 11.87 | 17.42 | 16.73 | 53.97 |
| | #7 | 17.74 | 8.03 | 19.61 | 54.62 |

| | | | ering perone dia | THE COL MODIFICATION | • |
|----------|-------------|-------------------|------------------|----------------------|-------|
| | | Moving | Standing | Sitting | Lying |
| 4 Weaks | Post-Radiat | cion Observations | | | |
| Dog | #3 | .7074* | 5.402** | 2.161 | .9408 |
| | #6 | 1.011 | 1.347 | 1.726 | .9444 |
| | #7 | .2802 | .3377 | .5808 | 1.617 |
| 12 Weeks | Post-Radia | ation Observation | s | | |
| Dog | #3 | .7607 | 1.705 | 10.14 | .6375 |
| | #6 | .9966 | 2.440 | 6.942 | .6872 |
| | #7 | .7235 | •5909 | 1.760 | 1.076 |

^{*}Numbers less than 1.0 indicate a decrease in the behavior after radiation.

**Numbers greater than 1.0 indicate an increase in the behavior after radiation.

 $^{^{\}text{A}}(\frac{\text{% time pre-radiation}}{\text{% time post-radiation}})$

- Test 3 increases in standing (145 minutes) and sitting (201 minutes)
 - decreases in lying (340 minutes)

Differences for dog 7 are as follows:

Test 2 - increases in lying (524 minutes)

- decreases in moving (179 minutes), standing (89 minutes),
 and sitting (37 minutes)
- Test 3 increases in sitting (140 minutes)
 - decreases in moving (32 minutes) and standing (42 minutes)

Two other comparisons also support the trend toward a drop in activity during test 2. The number of times dogs 6 and 7 jumped decreased, and both dogs had fewer major changes in activity (Table 2). In the twenty-four hours of test 2, dog 6 changed behaviors 191 fewer times than during the control test 1. Dog 7 changed 353 fewer times and continued the trend in test 3.

Overall, the three dogs, and particularly dog 7, showed an increase in sedimentary behaviors following radiation, in test 2. In test 3 the record time tended to shift from lying to standing and sitting. Motion did not change appreciably.

B. Maze Learning Studies.

Each of the twelve dogs was run through a predefined series of twelve mazes (Figure 3). One maze pattern was used each day with eight trials given each dog each day. The 24 x 24 foot square maze was marked off into 4 foot square sections and each time a new square was entered, it was counted. The total number of squares entered on each trial was subtracted from the minimum number of squares necessary to complete the maze. This error score for each trial of each dog is shown in Appendix 1. Test 1 was run prior to radiation, test 2 occurred approximately two weeks post-radiation, and test 3 took place

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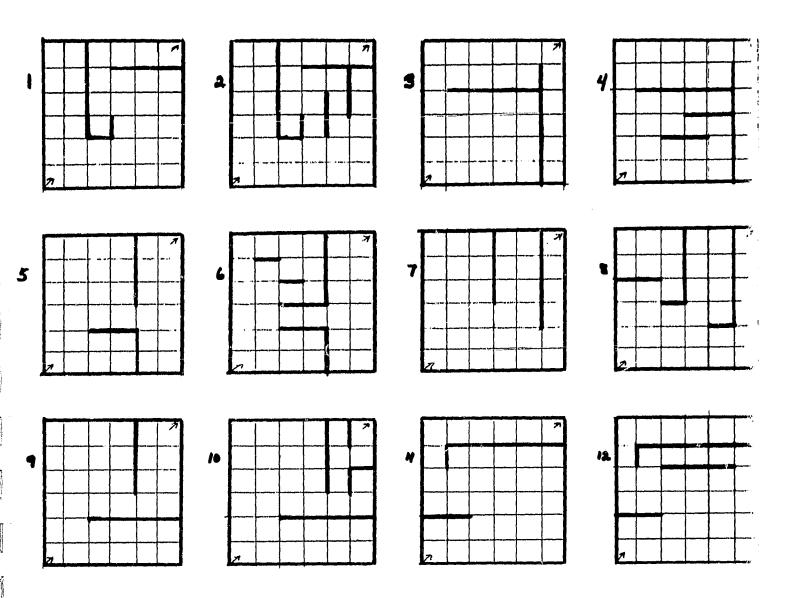


Figure 3. Maze Problems 1 - 12.

approximately eleven weeks post-radiation.

The total number of errors for all twelve dogs was 9522 on test 1, 3461 on test 2, and 1814 on test 3, indicating that learning did occur during the investigation. The small number of errors in test 3 make the error score data of that test relatively meaningless. This, however, was a result of the necessitated short time interval between tests.

Total mean errors is the result of dividing the total errors by the number of dogs. The non-radiated six control dogs (1, 2, 4, 9, 11, and 12) had mean errors of 798.7 on test 1, 282.8 on test 2, and 122.2 on test 3. The heavily radiated dogs (3, 6, and 7) had a total mean error score on test 1 of 771.3, essentially the same as that for the control beagles. In tests 2 and 3, however, the total mean errors, 398.7 and 173.0 respectively, were 41% higher than those for the control dogs. The radiated dogs made more errors than did the controls.

To determine when the errors were made, %R1, %R4, and %R5 scores were calculated. Of the total errors made during a test by a specific dog, the percentage of the errors occurring during the first trials each day (%R1) was determined by dividing the errors made in trial 1 by the total errors of the test (Table 5). The six control dogs and the three heavily radiated dogs both had pre-radiation %R1 values of approximately 31%. Thirty-one percent of the mistakes in test 1 occurred on the first trial, 69% occurred during the remaining 7 trials. During test 2 the groups were differentiated, with the control group having 34% of their errors in trial 1, while the radiated dogs made 19% of their errors the first time through. This means the second group had a larger proportion of their errors occurring in later trials. By test 3, the radiated dogs exceeded their test 1 %R1 score.

The percentage of the errors occurring in the first half of the trials,

| | Test 1 | Test 2 | Test 3 |
|-------------------|--------|--------|--------|
| Dog #1*B | 32.04 | 36.11 | 39.25 |
| #2* | 25.26 | 20.37 | 28.64 |
| #3** | 34.30 | 23.57 | 45.59 |
| #4* | 28.79 | 21.78 | 34.38 |
| #5 | 38.22 | 38.02 | 54.55 |
| #6** ^C | 27.58 | 18.59 | 33.98 |
| #7** | 32.69 | 14.31 | 35.48 |
| #8 | 29.89 | 32.95 | 35.38 |
| #9* | 36.41 | 31.65 | 42.86 |
| #10 | 38.46 | 49.26 | 37.14 |
| #11* | 37.40 | 59.34 | 29.73 |
| #12* | 22.61 | 34.09 | 29.17 |
| *Control group | 30.42 | 33.89 | 34.01 |
| *"Radiated group | 31.52 | 18.82 | 38.35 |

$$A(\%R1 = \frac{errors in Trial 1}{total errors} \times 100)$$

 $^{^{\}mathrm{B}}\mathrm{Dogs}$ 1,2,3,4,5,7,8, and 12 were males.

 $^{^{\}rm C}_{\rm Dogs}$ 6,9,10, and 11 were females.

RR4, was determined by dividing the total errors occurring in trials 1-4 by the total number of errors for each dog (Table 6). The control and radiated dogs had approximately equal RR4 scores in pre-radiation test 1, 74% and 79% respectively. While the six control beagles continued to score approximately the same on tests 2 and 3, the radiated dogs had a test 2 score which averaged 63.66% of what it was in test 2, and a test 3 score of 84.44% pre-radiation levels. The lowered RR4 scores indicate that the dogs were making a greater percentage of their mistakes in trials 6, 7, and 8. They were not learning the maze pattern as well as the control dogs.

The percentage of errors occurring in the first five trials, %R5, is shown in Table 7. The test 2 scores of the heavily radiated dogs were still lower than those for controls, although scores for test 3 had returned to more normal levels.

Odd numbered mazes were constructed so that the dogs could easily observe the maze solution. Even numbered mazes presented several alternatives for the animals. Table 8 compares the number of errors which occurred in the odd numbered visual problems. These represented approximately one-third of the errors. Non-visual, even numbered mazes proved more difficult, but there was no variation between the control and heavily radiated groups.

Overall, the three heavily radiated dogs made more errors on the maze learning study. These beagles also did not learn the maze patterns as well or as quickly as did the control dogs.

C. Behavioral Observations.

The pre-radiation phase of this study permitted the researchers to learn each dog's general personality. During the two post-radiation phases, it was then possible to notice whether changes occurred in individual dogs. Specific observations were recorded but their relationship to radiation doses

Table 6 The Percentage of Total Errors Committed in Trials 1-4 $(\$R4)^{\mbox{\scriptsize A}}$

| | | Test l | Test 2 | Test 3 |
|------|--------------|--------|--------|--------|
| Dog | #1*B | 62.41 | 86.15 | 64.49 |
| | #2* | 65.89 | 63.62 | 69.90 |
| | #3** | 87.97 | 54.51 | 74.71 |
| | #4* | 71.34 | 47.55 | 68.75 |
| | #5 | 81.00 | 77.60 | 81.82 |
| | #6**C | 81,17 | 50.00 | 64.08 |
| | #7** | 69.33 | 47.28 | 62.58 |
| | #8 | 83.98 | 76.88 | 69.31 |
| | #9* | 78.22 | 72.78 | 72.73 |
| : | #10 | 85.47 | 79.31 | 78.86 |
| | #11* | 86.70 | 78.57 | 67.57 |
| | #12* | 77.67 | 70.45 | 62.50 |
| *Co | ntrol group | 73.71 | 69.85 | 67.66 |
| **Ra | diated group | 79.49 | 50.60 | 67.12 |

 $A(\%R4 = \frac{errors in Trials 1-4}{total errors})$

 $^{\mathrm{B}}$ Dogs 1,2,3,4,5,7,8, and 12 were males.

 $^{\mathrm{C}}\mathrm{Dogs}$ 6,9,10, and 11 were females.

| | Test 1 | Test 2 | Test 3 |
|----------------------|--------|--------|--------|
| Dog #1* ^B | 76.42 | 91.54 | 71.03 |
| #2* | 70.53 | 69.02 | 82.04 |
| #3** | 91.22 | 75.20 | 81.99 |
| #4* | 80.89 | 61.96 | 75.00 |
| #5 | 92.62 | 84.90 | 88.18 |
| #6** ^C | 85.20 | 63.46 | 77.67 |
| #7** | 74.73 | 67.75 | 79.35 |
| #8 | 90.04 | 90.17 | 80.14 |
| #9* | 84.32 | 81.01 | 79.22 |
| #10 | 89.46 | 84.25 | 84.57 |
| #11* | 90.58 | 85.71 | 77.03 |
| #12* | 85.11 | 78.79 | 70.83 |
| *Control group | 81.31 | 78.01 | 75.86 |
| **Radiated group | 83.72 | 68.80 | 79.67 |

 $A(\%R5 = \frac{errors in Trials 1-5}{total errors} \times 100)$

 $^{^{\}mathrm{B}}\mathrm{Dogs}$ 1,2,3,4,5,7,8, and 12 were males.

 $^{^{\}mathrm{C}}\mathrm{Dogs}$ 6,9,10, and 11 were females.

| | | Test 1 | Test 2 | Test 3 |
|-------|-------------------|--------|--------|----------|
| Dog | #1*B | 29.82 | 29.62 | 37.38 |
| | #2* | 26.54 | 26.82 | 18.93 |
| | #3** | 19.98 | 18.24 | 19.16 |
| | #4* | 34.01 | 19.63 | 38.54 |
| | #5 | 32.14 | 5.21* | ** 36.36 |
| | #6** ^C | 32.74 | 30.77 | 42.72 |
| | #7** | 34.33 | 40.76 | 42.58 |
| | #8 | 35.18 | 29.48 | 37.18 |
| | #9* | 26.66 | 35.44 | 25.32 |
| 1 | #10 | 29.63 | 32.51 | 25.71 |
| = | #11* | 36.01 | 22.53 | 50.00 |
| ŧ | #12* | 52.39 | 22.73 | 34.38 |
| *Co | ntrol group | 34.24 | 26.13 | 34.09 |
| **Rac | diated group | 29.02 | 29.92 | 34.82 |

^{***}Dog was sick on 2 odd numbered and 1 even numbered tests

 $A_{(\%P = \frac{\text{errors on odd numbered visual problems}}{\text{total errors}} \times 100)$

 $^{^{\}mathrm{B}}$ Dogs 1,2,3,4,5,7,8, and 12 were males.

 $^{^{\}text{C}}\text{Dogs 6,9,10,}$ and 11 were females.

was not established until the conclusion of the study.

Test 2, occurring approximately two weeks post-radiation, had two dogs showing behavior changes from those observed in the initial study.

- 1) Dog 3, a heavily irradiated dog, had two days in which he was extremely fearful of the events associated with running the maze. A third day did not have the fear reaction, but there was a general lack of enthusiasm for the run. Subsequent days were normal, and no cause could be determined for the apparent expression of fear.
- 2) Dog 8, a low-dose irradiated beagle, was hospitalized for three days of intestinal upset with accompanying bloody and mucus-filled diarrhea. Recovery was uneventful.

Test 3 was held about eleven weeks post-radiation. Seven dogs showed slight to dramatic behavior changes when compared to their normals established earlier.

- 1) Dog 2, a control, became more enthusiastic about running through the maze and tended not to be distracted by odors.
- 2) Dog 3, a heavily irradiated dog, developed a severe head shake which occurred with almost every trial and while the dog was kenneled. The ear canals were normal when this problem started, and only after a couple of weeks of head shaking did they show signs of irritation and infection as a result of the head shaking. This same dog also changed from a very outgoing, social personality to one that became relatively indifferent to his environment and to the people working with him.
- 3) Dog 6, a heavily irradiated beagle, performed normally in the maze but was difficult to get out of the kennel area.
- 4) Dog 7, a heavily irradiated dog, also developed a severe head shake which lasted throughout the entire test period. As with dog 3, this dog's ear

canals were clean initially and only became irritated as a result of the head shaking. Dog 7 also had a dramatic personality change. He became much friendlier to people working with him, sought attention in the kennel area, and was almost eager to run the maze. Previously, he had been indifferent to people and lacked motivation to run the maze, often spending time just walking around in it.

- 5&6) Dogs 8 and 10, beagles which received the low dose of radiation, occasionally would shake their heads; however, the ear canals of both dogs were normal.
- 7) Dog 9, a low dose irradiated dog, would occasionally show a slightly fearful way of traveling through the maze.

Overall, two control dogs showed slight occasional changes of observable behavior. Two dogs receiving light doses of radiation developed occasional head shaking. All three heavily radiated dogs had some behavior changes, with two of them developing dramatic personality changes and severe head shaking not associated with ear infections.

IV. NEUROLOGIC STUDIES

Screening electroencephalograms were recorded on all dogs under general thiobarbiturate anesthesia on April 21, August 12, and September 8, 1982. All were determined to be normal for size and age.

Pre-irradiation neurologic examination on the same dates revealed no abnormalities in any of the dogs.

Post irradiation electroencephalograms were recorded on November 16, 1982 and again on January 19, 1983. No abnormalities were detected in either irradiated group or the control group. Neurologic examination again was normal for all groups. Representative EEG's are shown in Appendix IV.

Addirional evaluation of each dog by computed tomography (CT) scanning of

the skull was accomplished under thiobarbiturate anesthesia on January 19, 1983. There were no differences between irradiated dogs and the control dogs.

V. NUCLEAR MEDICINE STUDIES

All beagles included in these studies had brain scans performed prior to irradiation and twice post irradiation. In addition, a cerebral blood flow study was done during the second post-irradiation scan procedure. See Appendices II and III for details of the procedures.

Figure 4 is an example of a brain scan from a dog. Figure 5 is an example of a blood flow study in the same dog. Note that both carotid arteries can be visualized and that the brain is perfused quicker than other parts of the head. Figure 6 is a curve obtained by including the total brain in a computer region of interest and then plotting the time versus activity curve. Figure 7 is the same type of information but obtained from each half of the brain. Thus, a comparison can be made between sides. These are all shown to illustrate the type of data reviewed to reveal the presence of any anatomic or physiologic abnormality.

All data was reviewed in several ways. First, each was studied as a part of the series performed within a matter of 3 days. Next, all data on individual dogs was reviewed together. Lastly, all data from the irradiated groups and control group were reviewed together. No abnormality was detected by any of the data review procedures used.

These results are not surprising. Abnormalities resulting from whole brain irradiation will be expected to appear after a longer post irradiation period. This is the reason we are recommending that this group of dogs be retained for continued study.

VI. CONCLUSIONS

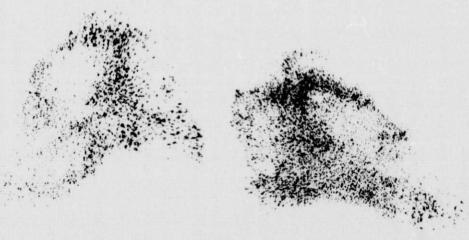
1. Dogs receiving the highest dose of radiation had decreased activity

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POSTERIOR



LEFT LATERAL

RIGHT LATERAL

Figure 4. Brain Scan of Beagle Dog #11, Control.

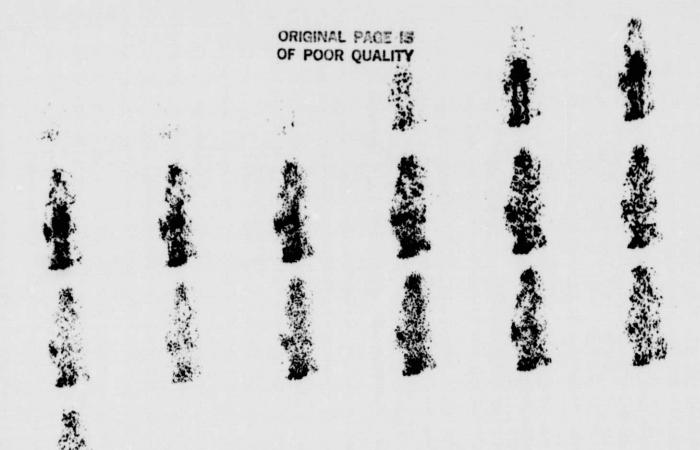


Figure 5. Blood Flow to Brain Study of Beagle #11, Control.

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Figure 6. Graph of Blood Flow to Total Brain of Beagle #11, Control.

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levels in the early weeks following irradiation.

- 2. Dogs receiving the highest dose of radiation made more errors in the maze tests than did unirradiated dogs.
- 3. Errors made in maze tests by dogs which had received radiation were spread throughout the tests indicating that the dogs did not learn the patterns as well as the control dogs.
- Personality changes did occur during later phases of the study in 2 of
 dogs receiving the highest dose of radiation.
- 5. Headshaking was observed during later phases of the study in 4 of 6 dogs which had been irradiated. This was not associated with inflammation of the external ear canal.
- 6. No evidence of abnormal blood flow to the brain nor discrete lesions were revealed by the nuclear medicine procedures.
 - 7. No significant changes were observed in the electroencephalograms.
 - 8. CT scans did not reveal any discrete brain lesions.
- 9. Evaluation procedures selected are appropriate for studies of this type.

VII. RECOMMENDATIONS

One would not ordinarily expect to obtain readily identifiable anatomic or physiologic defects/or deficits at the early times post irradiation and none were found. Behavioral changes can and do occur in the absence of these defects. Thus, we strongly recommend that evaluation procedures of the type decribed above continue to be used on these dogs. It is only then that definitive information will be forthcoming from this group of valuable experimental animals.

APPENDIX I

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APPENDIX II

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APPENDIX II

Procedure for Cerebral Blood Flow

Cerebral blood flows on the irradiated beagles were performed in order to study extracranial and intracranial blood flow. Through this procedure gross abnormalities in the physiology and anatomy of cerebral circulation can be revealed.

I. Materials

A. Instrumentation

- Maxicamera Scintillation Camera System (General Electric, Medical Systems Division, Milwaukee, Wisconsin)
- Med IV Series Computer System and Nuclear Medicine Software (General Electric, Medical Systems Division, Milwaukee, Wisconsin)
- B. Radiopharmaceutical (Imaging Agent)

Technetium-Gluceptate Complex

- a) Gluceptate Sodium Kit (Glucoscan) (New England Nuclear, North Billerica, Mass.)
- b) Sodium Pertechnetate (Tc 99m) obtained from ⁹⁹Mo→⁹⁹Tc generator (Mallinckrodt, St. Louis, Missouri)

II. Scanning Technique

- A. Program computer and camera formatter to acquire dynamic study
 - 1. Set computer to acquire 1 frame/second for 30 frames for quantitative evaluation.
 - 2. Set camera formatter to acquire 1 frame/2 seconds for 15 frames for qualitative evaluation.
- B. Position the cranium of the beagle in a vertex position in relation to the scintillation camera and secure in place to prevent movement.

Appendix II (cont'd)

II.

- C. Inject approximately 10 mCi of ^{99m}Tc-Gluceptate into cephalic vein of thoracic limb, being careful to keep it out of the camera's field of view.
- D. Simultaneously start acquiring cerebral flow data on the computer and camera formatter.

III. Analysis of Cerebral Blood Flow with Nuclear Medicine Software

- A. Display flow on CRT of computer.
- B. Create summed image from representative frames.
- C. Create region of interest of cerebral area on summed image.
- D. Generate curves of the region of interest for the entire flow period, store, and normalize.
- E. Display and print curves.
- F. Analyze curves.
 - 1. Calculate transit times
 - 2. Calculate slopes

APPENDIX III

APPENDIX III

Procedure for Static Brain Scan

Static brain scans were performed to demonstrate pathophysiologic changes in the brain accompanied by changes in the blood brain barrier. The radiopharmaceutical used penetrates into brain substance after a breakdown of the blood-brain barrier and is used to localize pathophysiological areas.

I. Materials

A. Instrumentation

- Maxicamera Scintillation Camera System (General Electric, Medical Systems Division, Milwaukee, Wisconsin)
- Med IV Series Computer System and Nuclear Medicine Software (General Electric, Medical Systems Division, Milwaukee, Wisconsin)
- B. Radiopharmaceutical (Imaging Agent)

Technetium-Gluceptate Complex

- a) Gluceptate Sodium Kit (Glucoscan) (New England Nuclear, North Billerica, Mass.)
- b) Sodium Pertechnetate (Tc 99m) obtained from ⁹⁹Mo→⁹⁹Tc generator (Mallinckrodt, St. Louis, Missouri)

II. Scanning Technique

- A. Inject approximately 10 mCi of ^{99m}Tc-Gluceptate into the cephalic vein of a thoracic limb.
- B. Delay 2 hours.
- C. Administer anesthetic agent or tranquilizer if necessary to prevent movement.
- D. Program computer and camera formatter to obtain 100,000 counts for each static image.

Appendix III (cont'd)

JI.

- E. Obtain 4 views
 - 1. Vertex
 - 2. Posterior
 - 3. Right lateral
 - 4. Left lateral

III. Analysis of Static Brain Images

- A. Display image on CRT of computer. Adjust contrast enhancement and background erase to enhance abnormal areas. Evaluate for abnormalities.
- B. Evaluate scintiphotos produced on camera formatter for abnormalities.

APPENDIX IV

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